

### **REMARKS**

Entry of the foregoing, reexamination and reconsideration of the subject application, as amended, pursuant to and consistent with 37 C.F.R. §1.116, are respectfully requested in light of the remarks which follow.

#### **I. Claim Amendments**

By the foregoing amendment, claims 1, 3, 5, 7, 17, 19, and 28 have been amended, and claims 2, 6, and 27 have been canceled.

Specifically, claims 1 and 5 have been amended by replacing the phrase "cells *derived* from an animal" with "cells *collected* from an animal," as supported at least at page 8, paragraph 21 of the specification.

Claims 1 and 5 have also been amended by deleting recitation of plants, organs of plants, and plant cells.

Claims 1 and 5 have been further amended to recite that the transgene is introduced using a viral vector. This amendment is supported throughout the specification and claims as filed, for example by original claim 2.

In addition, claim 1 has been amended to recite that the insulator from sea urchin arylsulfatase gene protects the transgene from silencing. Support for this amendment can be found at least at page 7, paragraph 18, and in the experiments.

Finally, claims 3, 7, 17, 19, and 28 have been amended to depend from non-canceled claims.

The amendments to the claims, including cancellation of claims, have been made without prejudice or disclaimer to any subject matter recited or canceled herein. Applicants reserve the right to file one or more continuation and/or divisional applications directed to any canceled subject matter. No new matter has been added, and entry of the foregoing amendments of the above-identified application are respectfully requested.

#### **II. Response to Claim Rejections Under 35 U.S.C. § 102 – Shinmyo et al.**

At pages 3 and 4 of the Office Action, claims 1, 4, 5 and 8 were rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Shinmyo et al. (U.S. 6,229,070).

Specifically, the Examiner indicated that the anti-silencing effect of the insulator is merely recited in the preamble of the present claim 1, and as such is not a limitation of the

claims. The Examiner further stated that the ArsI insulator recited in the present claims encompasses the ArsI insulator disclosed by Shinmyo et al.

To expedite prosecution and not to acquiesce to the Examiner's rejection, claims 1 and 5 have been amended to recite the limitations of claims 2 and 3 (*i.e.* introduction of the transgene via a viral vector). Because claims 2 and 3 are not included in the rejection over Shinmyo et al., the above-mentioned amendment to claims 1 and 5 should be sufficient to overcome this rejection.

Thus, Applicants respectfully request reconsideration and withdrawal of this rejection.

### **III. Response to Claim Rejections Under 35 U.S.C. § 103**

At page 4 of the Office Action, Claims 2, 3, 6, 7 and 17-20 were rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Shinmyo et al.

Specifically, the Examiner indicated that although Shinmyo et al. do not teach the claimed method wherein the transgene is introduced using a viral vector such as the lentiviral vector, lentiviral vectors are well known in the art and routinely used for introducing transgenes into cells.

This rejection is respectfully traversed, for at least the following reasons.

First, as noted in the response filed October 31, 2006 (*see* pages 8 and 9), Shinmyo et al. discloses that ArsI can serve as an insulator. However, the anti-silencing activity of ArsI is not taught or suggested in the reference. Because an insulator does not necessarily have anti-silencing activity, a person of ordinary skill in the art would not have reasonably expected, based on the reference, that ArsI would be able to protect a transgene from silencing.

Second, the description in Shinmyo et al. relates to plant cells (*i.e.* tobacco BY2 cells). To expedite prosecution and not to acquiesce to the Examiner's rejection, claims 1 and 5 have been amended by deleting recitation of plants, plant organs, and plant cells. Thus, the claims as amended are directed to methods for protecting a transgene from silencing in animals, animal organs, and animal cells. Applicants note that the mechanisms involved in silencing differ significantly between plants and animals. In plants, it is known that RNAi is the main phenomenon underlying silencing. However, DNA methylation and epigenetic change are important causes of silencing in animals. Further, the heterochromatin region, which plays a critical role in gene silencing in animal cells, is rare in the genome of plants.

Accordingly, any indication that ArsI might have anti-silencing activity in plants would not reasonably suggest that ArsI would be useful for preventing silencing in animals.

Third, the Shinmyo et al. transgene is introduced via an *Agrobacterium tumefaciens* mediated method, which is a conventional method utilized for the transformation of plants. The reference does not teach or suggest the retroviral vectors of the present invention, which are conventionally used for transformation of animals and for gene therapy.

For at least the reasons set forth above, Shinmyo et al. does not teach or suggest the methods recited in the present claims. Accordingly, Applicants respectfully request reconsideration and withdrawal of this rejection.

#### **IV. Response to Claim Rejections Under 35 U.S.C. § 101**

At page 4 of the Office Action, claims 1-8, 17-20, 27 and 28 were rejected under 35 U.S.C. § 101 for allegedly being directed to non-statutory subject matter.

It is the Examiner's position that because the present claims encompass introducing a transgene into a human, the claims read on the creation of a transgenic human. Thus, the Examiner concluded that the claims are directed to nonstatutory subject matter.

This rejection is respectfully traversed, for at least the following reasons.

According to the USPTO Manual of Patent Examining Procedure (MPEP), "[i]f the broadest reasonable interpretation of the claimed invention as a whole encompasses a human being, then a rejection under 35 U.S.C. § 101 must be made indicating that the claimed invention is directed to nonstatutory subject matter" (MPEP § 2105). The MPEP cites a USPTO Notice (Animals-Patentability, 1077 O.G. 24, April 21, 1987). The Notice, in turn, states that "[a] claim directed to or including within its scope a human being will not be considered to be patentable subject matter under 35 U.S.C. § 101." Thus, USPTO policy prohibits the patenting of "human beings." However, the Examiner has not provided any authority for the position that a method that may "read on the creation of a transgenic human" (Office Action, page 4) is directed to non-statutory subject matter.

Applicants respectfully submit that the present claims do not read on nonstatutory subject matter, because the claims do not include within their scope a transgenic human being, or any human being. In contrast, the present claims are directed to methods for introducing a transgene, in particular for the purpose of gene therapy. Accordingly, the

claims recite patentably subject matter, and Applicants respectfully request reconsideration and withdrawal of this rejection.

**V. Response to Claim Rejections Under 35 U.S.C. § 102 – Akasaka et al.**

At page 5 of the Office Action, claims 27 and 28 were rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Akasaka et al. (Cellular and Molecular Biology (1999) 45, 555-569).

Specifically, the Examiner stated that Akasaka et al. disclose a method of introducing a sea urchin arylsulfatase insulator gene and a transgene into the human HeLa cell line (citing page 560, first column and third paragraph, and Fig. 5).

This rejection is respectfully traversed, for at least the following reasons.

It is well established that for prior art to be anticipatory, every element of the claimed invention must be disclosed in a single item of prior art in the form literally defined in the claim. *See, e.g., Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 213 U.S.P.Q. 81, 90 (Fed. Cir. 1986). Applicants submit that the cited reference fails to satisfy this requirement, for at least the following reasons.

The present claims recite methods for protecting a transgene from silencing. Applicants submit that in contrast to the present invention, the methods described in Akasaka et al. do not protect a transgene from silencing.

In support of this position, Applicants submit herewith a Gene Therapy paper, authored by the present inventors, among others, and published after the filing date of the present invention (Hino et al., Gene Therapy (2004) 11, 819-828). This paper includes the experiments set forth in the present application, showing the antisilencing effects of ArsI on lentiviral vectors, and provides further results demonstrating that ArsI protects lentiviral vectors from position effect variegation regardless of its orientation (*see, e.g.*, abstract and page 822).

In addition, Applicants provide evidence establishing that the anti-silencing effect obtained by the present methods is not inherent in Akasaka et al. The experimental results are presented in the Declaration of Dr. Tajima, submitted herewith. Applicants also submit a Declaration of Dr. Matsuoka, providing an opinion with regard to the experimental results. As noted in the Declaration of Dr. Matsuoka, the results of the experiments reported in the Declaration of Dr. Tajima demonstrate that the experimental system described in Akasaka et

al. does not provide an anti-silencing effect in the presence of a sea urchin arylsulfatase insulator. Thus, the experiments show that the anti-silencing effects provided by the methods recited in the present claims are not inherent in Akasaka et al.

Accordingly, the reference does not teach or even suggest the subject matter recited in the present claims, and Applicants respectfully request reconsideration and withdrawal of this rejection.

**VI. Response to Claim Rejections Under 35 U.S.C. § 112**

At pages 5 and 6 of the Office Action, claims 1-8, 17-20, 27 and 28 were rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite.

Specifically, the Examiner stated that the word "derived" in claims 1 and 5 renders the claims indefinite, because the number and nature of the derivative process is unknown.

In response, Applicants note that it is not clear what the Examiner means by the "*number* of the derivative process." However, with regard to the *nature* of the derivative process, the specification indicates that "cells derived from the living body" means "cells collected from the living body" (*see* page 8, paragraph 21). As noted above, the claims have been amended accordingly, by replacing the phrase "cells *derived* from an animal" with "cells *collected* from an animal."

Applicants submit that a person of ordinary skill in the art would readily recognize what is meant by "cells collected from an animal." Accordingly, Applicants respectfully request reconsideration and withdrawal of this rejection.


**CONCLUSION**

It is respectfully submitted that all rejections have been overcome by the above amendments. Thus, Notice of Allowance is respectfully requested.

In the event that there are any questions relating to this paper, or the application in general, the Examiner is respectfully urged to telephone Applicants' undersigned representative so that prosecution of this application may be expedited.

Respectfully submitted,

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